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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,912	10/04/2004	Takahiro Ito	0020-5301PUS1	4489

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
12/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/509,912	ITO ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-23 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-23 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 27 Aug 2009, in which claims 20, 21, 22, 23 and 25 are amended to change the scope and breadth of the claim and claims 24 and 31-34 are canceled.

The instant application is the 371 national stage entry of PCT/JP03/04745, filed 15 Apr 2003; and claims benefit of foreign priority document JP 2002- 112864, filed 16 Apr 2002; an English language translation of this foreign priority document has been made of record and the claim of foreign priority is perfected.

Claims 20-23 and 25-30 are pending and examined on the merits herein.

Objections Withdrawn

Applicant's Amendment, filed 27 Aug 2009, with respect to objection to the specification over a minor informality has been fully considered and is persuasive, as the amended specification at page 5, line 13 does not recite "mercapt group".

This rejection has been **withdrawn**.

Rejections Withdrawn

Applicant's Amendment, filed 27 Aug 2009, with respect to claims 20-23 and 30-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been fully considered and is persuasive, as

amended claims 20- 23 do not recite the genus of substituted lower alkyl group wherein the substituent is unlimited.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 27 Aug 2009, with respect to claims 20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Harada et al. (Journal of Controlled Release, 2000, 69, p399-412, of record) has been fully considered and is persuasive, as Harada et al. discloses a liquid preparation consisting of more than the elements recited in amended claims 20 and 22.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 27 Aug 2009, with respect to claims 21 and 23-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harada et al (Journal of Controlled Release, 2000, 69, p399-412, of record) in view of the '817 Patent (US Patent 5,340,817, issued 23 Aug 1994, of record) and in view of the '072 Patent (US Patent 6,288,072, issued 11 Sep 2001, of record) has been fully considered and is persuasive, as Harada et al. discloses a liquid preparation consisting of more than the elements recited in amended claims 21 and 23 and the '817 Patent and the '072 Patent do not remedy this teaching of Harada et al.

This rejection has been **withdrawn**.

The following are new grounds of rejection necessitated by Applicant's Amendment, filed 27 Aug 2009, in which claims 20, 21, 22, 23 and 25 are amended to change the scope and breadth of the claim and claims 24 and 31-34 are canceled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Amended Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Okuno et al. (Cancer Research, 2000, 60, p2988-2995, cited in PTO-892).

Okuno et al. discloses a liquid composition comprising T-0128 in a 0.2M phosphate buffer at pH 6.9 in water at a content of 4.5-5.5% w/w (page 2989, left column, section Characterization of T-0128). The compound T-0128 (page 2989, Figure 1 at bottom of page) meets the limitation of the instant camptothecin derivative. For an aqueous composition, 4.5-5.5% w/w is approximately 4.5-5.5% w/v because the density of water is 1 g/1 mL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okuno et al. (Cancer Research, 2000, 60, p2988-2995, cited in PTO-892).

Okuno et al. discloses a liquid composition comprising T-0128 in a 0.2M phosphate buffer at pH 6.9 in water at a content of 4.5-5.5% w/w (page 2989, left column, section Characterization of T-0128). The compound T-0128 (page 2989, Figure 1 at bottom of page) meets the limitation of the instant camptothecin derivative. For an aqueous composition, 4.5-5.5% w/w is approximately 4.5-5.5% w/v because the density of water is 1 g/1 mL.

Okuno et al. does not specifically disclose said composition consisting of (b) one or more salts selected from the group including an alkali metal chloride (instant claim 22).

Okuno et al. teaches a liquid composition comprising T-0128 dissolved in 0.9 % NaCl solution (page 2990, left column, paragraph 1) and in PBS, or phosphate buffered saline, at pH 7.0 (page 2290, right column, second full paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teaching of Okuno et al. to give a liquid composition comprising T-0128 in PBS at pH 7.0 at a concentration of approximately 4.5-5.5% w/v. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." See MPEP 2144.06 I.

Amended Claims 20, 22 and 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okuno et al. (Cancer Research, 2000, 60, p2988-2995, cited in PTO-892) in view of Harada et al. (Journal of Controlled Release, 2000, 69, p399-412, of record)

Okuno et al. discloses and teaches as above.

Okuno et al. does not specifically disclose or teach a composition having an ionic strength of 0.2 or less than 0.2 (instant claim 25).

Harada et al. teaches a liquid preparation comprising the camptothecin analog T-0128 and an acetate buffer, reduced glutathione, EDTA, and Triton X-100, which are stabilizers or fillers, adjusted to pH 7 using acetate or phosphate buffers, optionally with $CaCl_2$, an alkaline earth metal chloride, added (page 402, right column, section 2.4. *In vitro evaluation of drug release*). Harada et al. teaches the acetate or phosphate buffers are disclosed at a concentration of 40 mM (page 402, right column, section 2.4. *In vitro evaluation of drug release*), which gives an ionic strength of less than 0.2.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Okuno et al. in view of Harada et al. Both Okuno et al. and Harada et al. are drawn to liquid preparations containing the camptothecin analog T-0128 and a buffer. It would have been well within the level of ordinary skill in the art to optimize the ionic strength of the solution within prior art conditions. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical, see MPEP 2144.05 II.A. The evidence provided by Applicant is not drawn to the ionic strength of the liquid preparation, therefore there is no evidence indicating such concentration is critical.

Amended Claims 20-23 and 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okuno et al. (Cancer Research, 2000, 60, p2988-2995, cited in PTO-892) in view of Harada et al. (Journal of Controlled Release, 2000, 69, p399-412, of record) and further in view of Inoue et al. (WIPO Publication WO97/46260, published 11 Dec 1997, cited in PTO-892) and in view of the '817 Patent (US Patent 5,340,817, issued 23 Aug 1994, of record). As the WIPO Publication WO97/46260 is in Japanese, the national stage application issued as US Patent 6,436,912 is provided as an English-language equivalent and referenced as Inoue et al. herein.

Okuno et al. in view of Harada et al. teaches as above.

Okuno et al. in view of Harada et al. does not specifically teach the liquid composition consisting of one or more stabilizers selected from an alkali metal

carbonate and an alkali metal hydrogen carbonate (instant claims 21 and 23). Okuno et al. in view of Harada et al. does not specifically teach a lyophilized drug composition which is prepared by lyophilizing said liquid preparation (instant claim 29).

Inoue et al. teaches drug complexes comprising a drug compound bound to a carboxylalkyl dextran by means of a spacer comprising peptide-bounded amino acids (abstract). Inoue et al. teaches said drug includes camptothecin or derivatives thereof (column 6, lines 20-30). Inoue et al. teaches said spacer comprising glycine-glycine-glycine (column 8, lines 30-35). Inoue et al. teaches said drug complexes in the form of a lyophilized product and pharmaceutical additives such as solubilizers, pH modifiers and stabilizers available in the field of the art can be used (column 13, lines 55-65).

The '817 Patent teaches a camptothecin analog that is a water-soluble derivative of camptothecin bound to an amino acid or peptide (column 8, lines 19-22) "incorporated into a solution or suspension. The solutions or suspensions may also include the following components: a sterile diluent such as water for injection, saline solution... buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose." (column 13, lines 14-27). The '817 Patent also teaches oral liquid compositions of a camptothecin analog, such as capsules, elixirs, suspensions, syrups, which generally include an inert diluent or an edible carrier and incorporated with excipients (column 13, lines 29-36). The '817 Patent teaches the lyophilization of liquid preparations to provide the camptothecin derivatives (column 18, lines 30-31 and 52-53). The '817 Patent teaches the

camptothecin compound is compatible in solution with sodium bicarbonate, an alkali metal hydrogen carbonate (column 18, lines 15-20 and 40).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Okuno et al. in view of Harada et al. and further in view of Inoue et al. and in view of the '817 Patent. All of Okuno et al., Harada et al. and Inoue et al. are drawn to drug complexes comprising a drug compound bound to a carboxylalkyl dextran by means of a spacer comprising peptide-bounded amino acids, said drug encompassing camptothecin derivatives. All of Okuno et al., Harada et al. and the '817 Patent are drawn to camptothecin derivatives. One of ordinary skill in the art would have a reasonble expectation of success in combining Okuno et al. in view of Harada et al. and further in view of Inoue et al. and in view of the '817 Patent because Inoue et al. teaches pharmaceutical additives available in the field of the art can be used with the drug complexes taught by Inoue et al. and the '817 Patent teaches pharmaceutical additives compatible with camptothecin derivatives.

Response to Applicant's Remarks:

Applicant's Remarks, filed 27 Aug 2009, in view of evidence provided by the previously filed ITO Declaration have been carefully considered and not found to be persuasive.

Applicant notes that the '817 Patent discloses a camptothecin compound lacking a polysaccharide. Newly cited Inoue et al. teaches combining pharmaceutical additives available in the field of the art with the drug complex taught by Inoue et al. Therefore

one of ordinary skill in the art would have a reasonable expectation of success in combining solubilizers, pH modifiers and stabilizers as taught by the '817 Patent.

Applicant notes the evidence provided by the previously filed ITO Declaration compares the instant invention to a composition comprising sorbitol as disclosed in EP1308171. However, none of Okuno et al. in view of Harada et al. and further in view of Inoue et al. and in view of the '817 Patent require a sugar or sugar alcohol. Therefore Applicant's Remarks, filed 27 Aug 2009, in view evidence provided by the previously filed ITO Declaration are not persuasive with regards to the combination of Okuno et al. in view of Harada et al. and further in view of Inoue et al. and in view of the '817 Patent.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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